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Morphogenesis of bulboventricular malformations
II. Observations on malformed hearts

R. H. Anderson, J. L. Wilkinson, R. Arnold, A. E. Becker, and K. Lubkiewicz[1]

From the Department of Child Health, University of Liverpool, and the Department of Pathology, Wilhelmina Gasthuis, University of Amsterdam, Amsterdam, The Netherlands

The results are described of an investigation of specimens with bulboventricular malformations. The hearts examined had been previously classified as Fallot's tetralogy, double outlet right ventricle, or various forms of transposition. After re-examination of the specimens, it was concluded that they represented a spectrum of malformations. While some were typical of the 'classical' description of known anomalies, others had features intermediate between two 'classical' anomalies. Yet others were considered to be examples of recently described anomalies such as 'posterior' transposition or double outlet left ventricle. We believe that the spectrum of anomalies can be directly interpreted in terms of variation in position of the embryological components of the bulboventricular loop. These components were described in detail in the first part of this study which was devoted to development in the normal heart, and are defined as the conoventricular flange, the conus septum, the trabecula septomarginalis, and the anterior and posterior segments of the muscular ventricular septum. Our findings support the recent hypothesis that the spectrum can be explained in terms of conal rotation and conal absorption, but additionally suggest that reorientation of the anterior part of the muscular septum is a vital part of the process. The conclusions are discussed with regard to controversies concerning bulboventricular morphogenesis and nomenclature of supraventricular muscle bands of the right ventricle.

In the first part of our investigation (Anderson *et al.*, 1974) we suggested that a process of differential conal absorption was responsible for the production of the normal ventricular outflow tracts, and endorsed the findings of Goor, Dische, and Lillehei (1972) relative to the role of normal 'inversion' of the conus. We agreed with these investigators that a hypothetical situation with lack of this conal inversion could produce an embryonic heart approximating to the cardiac malformation of double outlet right ventricle, and that subsequent differential conal absorption from this situation would result in the anomaly of transposed great arteries.

Since we completed the first part of our study Goor and Edwards (1973) have described the results of an investigation of congenitally malformed hearts in which they demonstrated several specimens considered to be intermediate in morphology between double outlet right ventricle and complete transposition, and postulated that the two malformations constituted either end of an anomalous spectrum. This finding further endorsed the hypothesis that transposition represents conal maldevelopment, as promoted by Van Praagh and his associates (Van Praagh and Van Praagh, 1966; Van Praagh *et al.*, 1971; Van Praagh, 1973a, b). Other investigators, however, while accepting that double outlet right ventricle represents conal maldevelopment do not believe that transposition is an extension of this process. Instead they consider that truncal maldevelopment is necessary to produce transposed arteries (Van Mierop and Wiglesworth, 1963a, b; Van Mierop and Gessner, 1972). This latter concept has been endorsed by a recent investigation of specimens corresponding to the 'intermediate' forms of Goor and Edwards (1973). Angelini and Leachman (1973), however, considered the specimens to represent a distinct morphological entity, and to be quite different from complete transposition specimens.

This part of our investigation gives an embryological interpretation of an extensive collection of bulboventricular malformations.

Included in the specimens studied were examples

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[1]Present address: Montreal Children's Hospital (formerly Lecturer in Child Health, University of Liverpool).

of the controversial 'intermediate' forms described by both Goor and Edwards (1973) and Angelini and Leachman (1973). We shall, therefore, describe the anatomical configuration of all the hearts studied in terms of the embryological structures delineated in the first part of this study (Anderson *et al.*, 1974). We will then review our findings relative to the 'conal' and 'truncal' hypotheses concerning transposed arteries and to other controversial topics in the nomenclature of congenital heart disease.

Subjects and methods

The specimens studied were taken from the pathological collections of the Royal Liverpool Children's Hospital and the Pathology Department, Wilhelmina Gasthuis, University of Amsterdam. In each centre the hearts catalogued as Fallot's tetralogy, double outlet right ventricle, and transposition were studied, and after reclassification (see Fig. 1) the specimens were classified as indicated in the Table. In each group of malformations we delineated the position of the following embryonic components of the heart tube (Fig. 2): 1) bulboatrioventricular ledge, 2) conus septum, 3) trabecula septomarginalis, 4) posterior and anterior segments of the muscular septum, and 5) position and form of ventricular septal defects. Each of these components will be defined below.

We then compared the interrelation of the various structures in both the malformed specimens and a series of normal hearts. The pathological hearts (Table) have been classified according to the following criteria.

A: Fallot's tetralogy (Fig. 1A)

In addition to having dextroposition of the aorta, ventricular septal defect, pulmonary stenosis, and right ventricular hypertrophy, these hearts were also required to possess mitral-aortic fibrous continuity.

B: Double outlet right ventricle (Fig. 1B)

These hearts were required to possess a muscular ridge between the mitral and aortic valves. This ridge usually extended also between aortic and tricuspid valves; these hearts were described as possessing a *bilateral conus*. However, in some specimens of double

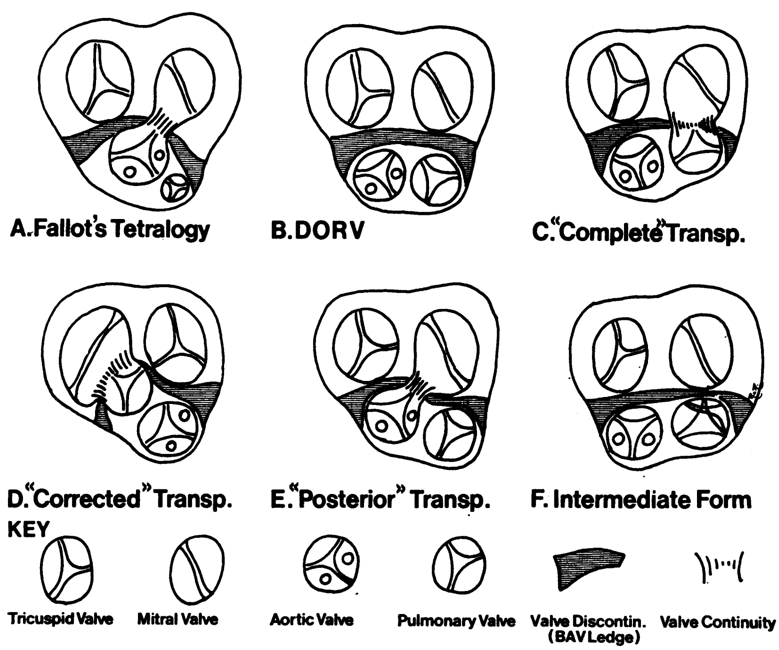


FIG. 1 *Diagram illustrating the groups into which the specimens studied were classified for descriptive purposes. Intermediate forms were in fact recognized between each of the subgroups, but only the intermediate (F) between double outlet right ventricle (DORV) and 'complete' transposition is illustrated. BAV = bulboatrioventricular (ledge).*

The form of posterior transposition (E) is unusual in that the illustrated mitral-aortic fibrous continuity occurs through a ventricular septal defect. The arteries are separated in this anomaly so that the aorta arises from the right ventricle and the pulmonary artery from the left.

TABLE *Classification of specimens studied*

Anomaly	*Definition*	*Subgroups*
Fallot's tetralogy	RV hypertrophy; ventricular septal defect; overriding aorta; pulmonary stenosis; mitral-aortic fibrous continuity	
Double outlet right ventricle	More than $1\frac{1}{2}$ arteries arising from right ventricle with mitral – semilunar valve discontinuity	a) With subaortic defect b) With subpulmonary defect c) With defect beneath both arteries (uncommitted)
Transposition	Aorta above morphological right ventricle; more than $\frac{1}{2}$ of pulmonary artery above left ventricle	a) With concordant AV relation (classically complete transposition) b) With discordant AV relation (classically corrected transposition) c) With concordant AV relation and apparently normally related arteries (posterior transposition)
Intermediates	Borderline specimens between any of above groups	a) Between double outlet right ventricle with subpulmonary defect and complete transposition b) Between double outlet right ventricle and double outlet left ventricle c) Between Fallot's tetralogy and double outlet right ventricle with subaortic defect and pulmonary stenosis

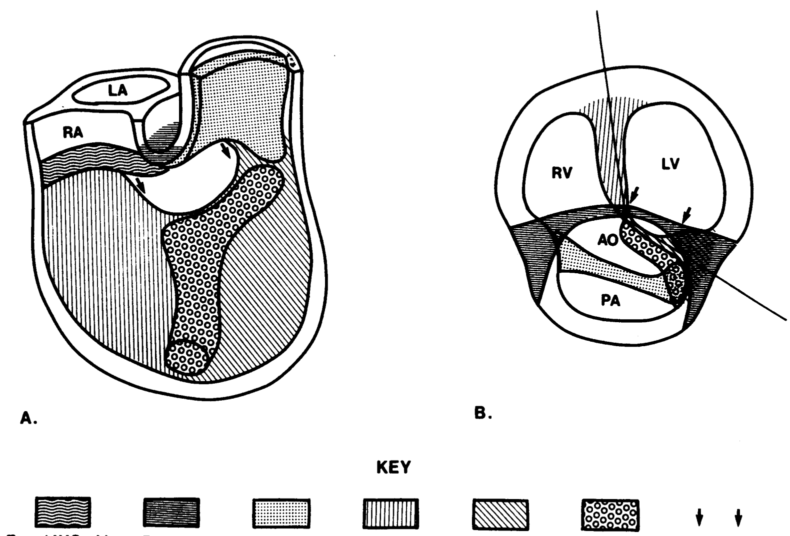


FIG. 2 *Representation of the embryonic heart tube after looping (see Anderson* et al. *(1974) for details).*

The five components which were delineated in the malformed hearts are indicated. They are posterior part of interventricular septum (post. segment); anterior part of interventricular septum (ant. segment); conus septum; bulboatrioventricular ledge (BAV ledge); and trabecula septomarginalis (trabecula SM). The extent of the primary foramen (BVFor.) is indicated by the arrows.

A) is a sagittal section viewed from the right and B) is a transverse section. LA, left atrium; RA, right atrium; LV, left ventricle; RV, right ventricle; AO, aorta; PA, pulmonary artery.

outlet right ventricle tricuspid-aortic fibrous continuity was present.

C: Transpositions

We took the recent definition of Van Praagh *et al.* (1971) as our criterion for this category. Thus we required that both great vessels should be placed across the ventricular septum so that they arose from their morphologically inappropriate ventricles. We were then able to describe three subgroups within this definition.

I: **With concordant atrioventricular relations** (classical complete transposition) (Fig. 1C).
II: **With discordant atrioventricular relations** (classical corrected transposition) (Fig. 1D).
III: **With concordant atrioventricular relations and normally related, transposed great arteries** (posterior transposition) (Fig. 1E).

In this latter category of posterior transposition, it should also be appreciated that mitral-aortic fibrous continuity was present through a ventricular septal defect. This is the rarest form of transposition, and a more complete description of the specimens presently studied is to be given elsewhere (Wilkinson *et al.*, in preparation).

Certain hearts could not be placed exactly into these rigid definitions, particularly when the pulmonary artery was positioned directly above the anterior ventricular septum. These hearts will therefore be described as *intermediate specimens* (Fig. 1F).

Definition of terms

The embryonic components of the primitive heart tube delineated in our previous study (Anderson *et al.*, 1974) are defined as follows:

A) Bulboatrioventricular ledge

This structure is the ridge produced on the endocardial surface of the heart tube by the bulboatrioventricular groove. It represents the inner curvature of the bulboventricular loop (Fig. 2). In the normal heart its middle portion is absorbed to allow the aorta to reach the left ventricle, and produces mitral-aortic continuity (Fig. 3).

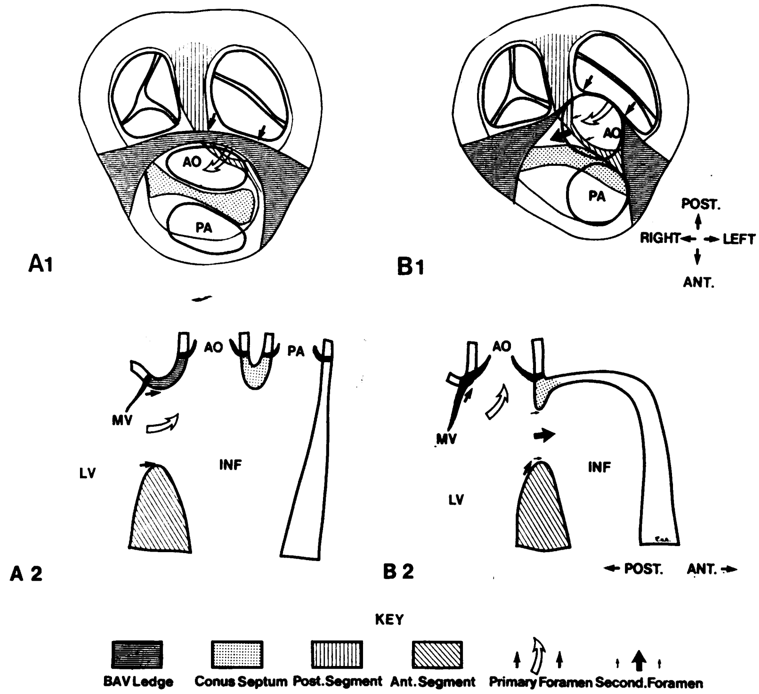


FIG. 3 *Diagrams illustrating the mode of formation of the aortic outflow tract by absorption of the mid-portion of the bulboatrioventricular ledge. A1 and 2 are transverse and sagittal sections before absorption, and B1 and 2 are comparable sections after absorption. Note that the primary foramen becomes reoriented to form the outflow tract, and the secondary foramen is formed between the conus septum and the tip of the muscular septum. It is the secondary foramen which is closed by the membranous septum. MV, mitral valve; INF, infundibulum. Other abbreviations as for Fig. 2.*

Its right margin separates the tricuspid and pulmonary valves, and together with the right column of the bulbar septum (q.v.) forms the normal crista supraventricularis (Fig. 4).

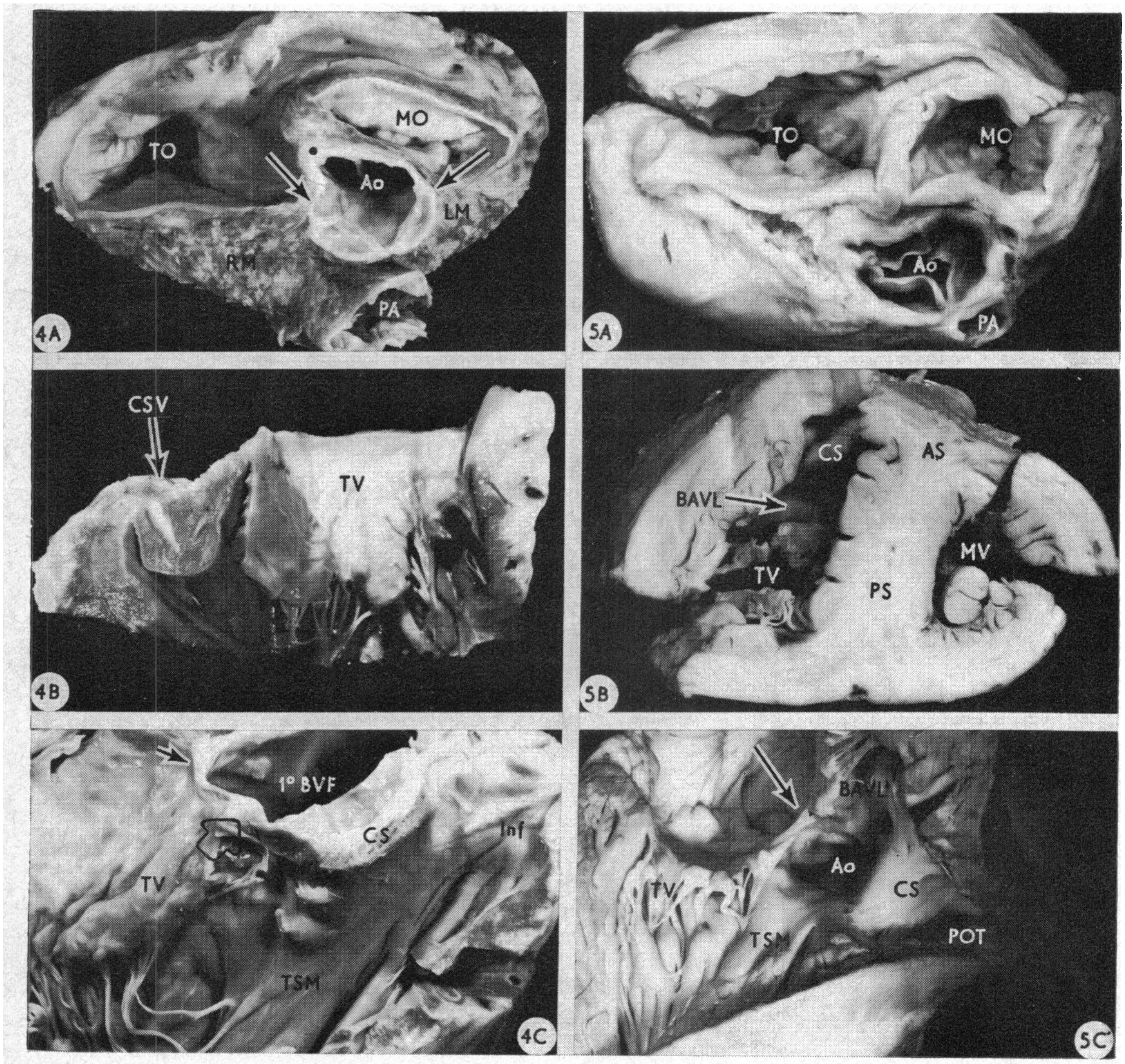
B) Conus (bulbar) septum

This structure represents the free proximal edge of the fused bulbotruncal swellings (Fig. 2). Though in the first part of our study we avoided the term '*conus*', it has such widespread clinical usage that we are now adopting it to describe our '*distal bulbus*'.

In the normal heart the conus septum is mostly incorporated into the interventricular septum, where it forms the anterior boundary of the secondary interventricular foramen (q.v.) (Fig. 3 and 4). However, its right-sided portion underlies the bulboatrioventricular ledge, and with it forms the normal *crista supraventricularis* (Fig. 4). From this position a well-formed trabeculation usually runs down the parietal wall of the right ventricle and joins the trabecula septomarginalis (Fig. 4).

C) Trabecula septomarginalis

This structure is an extensive septal trabeculation of the right ventricle (Fig. 2 and 4). It is usually an easy matter to strip this structure from the muscular ventricular septum in the normal heart. Superiorly it divides into two limbs, the main portion of the conus septum fusing with the muscular septum between them. The papillary muscle of the conus arises from the posterior limb. The body of the trabecula extends towards the ventricular apex where it gives rise to the anterior papillary muscle



and the moderator band (Fig. 4C). It then fuses with the parietal trabeculation from the crista, and forms an annulus between the right ventricular sinus and the infundibulum. It should be considered synonymous with the septal band (Van Praagh, 1968).

D) Muscular septum

This is the main muscular mass separating the ventricular cavities. In the normal heart it is divisible into two segments (Fig. 2). The posterior segment interposes between the ventricular inflow tracts and is oriented in the sagittal plane of the heart. The anterior segment separates the left ventricle from the infundibulum and is in the frontal plane of the heart.

The membranous septum of the normal heart is present between the two segments (Fig. 4).

E) Interventricular foramina

During formation of the bulboventricular loop, the original communication between ventricular and bulbar segments becomes obliquely oriented as the primary bulboventricular foramen. After formation of the posterior interventricular septum and lateralization of the right atrioventricular canal, the left side of the primary foramen persists as the only exit from the newly formed left ventricle (Fig. 3A). After differential conal absorption in the normal heart, the upper border of the foramen is absorbed to allow the aorta to move above the left ventricle, and thus the primary foramen becomes reoriented as the aortic outflow tract.

It follows that as the reoreintation occurs, a new obliquely oriented foramen is formed between the aortic outflow tract and the right ventricle (Fig. 3B). This new foramen is the secondary interventricular foramen, and its anterior boundary is the conal septum, which has been incorporated into the ventricular septum during the process of conal absorption. The secondary foramen is usually closed by growth from the endocardial cushions which forms the interventricular portion of the membranous septum. Should this closure not occur, then the persisting interventricular defect will be referred to as a *secondary defect*. However, should the conus itself not be absorbed, and hence the primary foramen not be reoriented, then any interventricular defect will represent part of the original bulboventricular foramen, and will be referred to as a *primary defect*.

Descriptions of specimens

For the purpose of this investigation, the pathological specimens will be described as though the heart were in the upright position, with atrial chambers being considered superior to ventricular chambers. We appreciate

FIG. 4 *Photographs of normal hearts. Fig 4A is dissected to demonstrate the persisting right (RM) and left (LM) margins of the bulboatrioventricular ledge (BAVL), and the absorbed portion* (between arrows). *The absorbed portion itself is divided into two segments, the right segment to the dot is the membranous septum, the left segment is the area of mitral-aortic fibrous continuity. Note that the absorptive process has carried the aortic valve (Ao) into a deep wedge position between the tricuspid (TO) and mitral (MO) orifices. Note also that the pulmonary artery (PA) is anterior and to the left of the aorta. Fig. 4B is the parietal wall of the right ventricle removed by a cut through the mid-sagittal plane of the tricuspid valve (TV). The wall is viewed from the septal aspect, and the pulmonary outflow tract remained in the septal portion of the heart. The crista supraventricularis (CSV) is demonstrated, and its two components are clearly delineated. One is the outer wall of the heart (BAVL), the other is the parietal extension of the conus septum. Fig. 4C is the septal portion of a heart bisected as in Fig. 4B, but viewed from its parietal aspect. The absorbed BAVL can be seen surrounding the reoriented primary foramen (1°BVF), and atrial* (closed arrow) *and ventricular* (open arrow) *segments of the membranous septum are demonstrated. The ventricular segment is bounded anteriorly by the conus septum (CS), itself fusing with the anterior septum (Inf.) between the limbs of the trabecula septomarginalis (TSM). TV, tricuspid valve.*

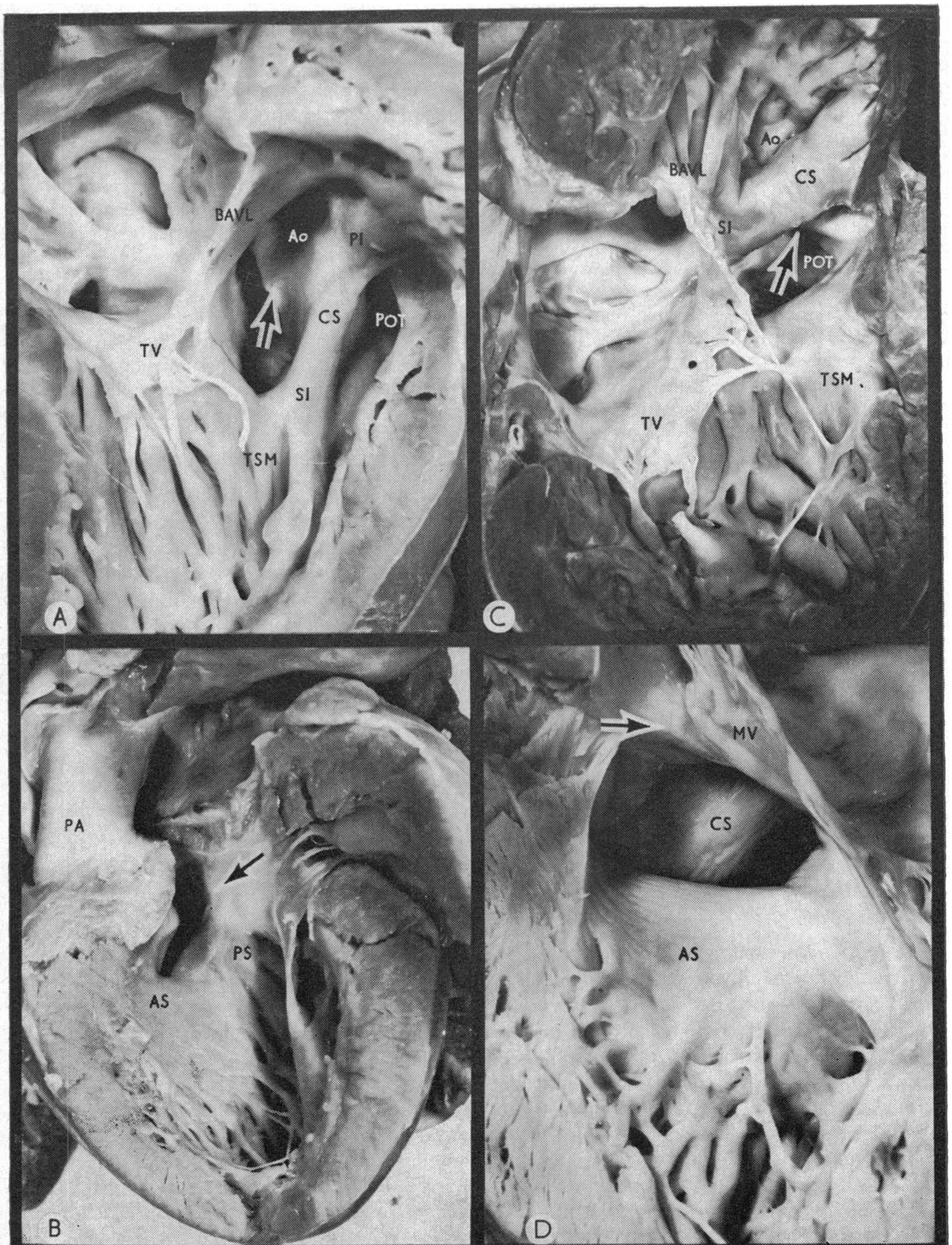
FIG. 5 *Photographs of specimens of Fallot's tetralogy. Fig. 5A and 5B are superior and inferior views of the atrioventricular junctional regions. In 5A the rotation of the conus is demonstrated by the dextroposition of the aorta (Ao) and its anterior deviation from the wedge position (Cf. Fig. 4A). Fig. 5B shows that the bulboatrioventricular ledge separates the tricuspid valve (TV) from the dextroposed aortic valve, while the conus septum (CS) separates the latter from the pulmonary outflow tract. Note the divorce of conus septum from bulboatrioventricular ledge, with the production of two supraventricular muscle masses. The anterior and posterior (PS) parts of the ventricular septum are both hypertrophied. MV, mitral valve. Fig. 5C is a view of the right ventricle from its apex looking towards the pulmonary outflow tract (POT). Note that the conus septum is deviated anteriorly, and is inserted in front of the trabecula septomarginalis (TSM). Note also that the right margin of the bulboatrioventricular ledge is absorbed to permit tricuspid-aortic valvular continuity* (arrow). *(Cf. Fig. 4C.)*

that this is not the position the heart occupies during life, and may cause confusion. However, the main purpose of the present investigation is to compare directly the morphology of individual hearts, and therefore a standard 'position' for the heart was required. It is hoped to correlate the established morphology of the various malformations with angiographic appearances in a future presentation

Results

A: Normal hearts

In the normal condition the aortic valve is posterior and slightly to the right of the pulmonary valve (Fig. 4A). Examination of the bulboatrioventricular ledge indicates that it has been extensively absorbed in its middle portion so that the aorta is above the



left ventricle (Fig. 4). However, the anterior part of the valve overrides the ventricular septum. The conus septum is in two portions. That part between the great arteries is incorporated into the muscular ventricular septum, and forms the anterior boundary of the membranous septum (Fig. 4). From this septal portion, the conus septum extends to the parietal wall of the right ventricle, and underlies and fuses with the right margin of the bulboatrioventricular ledge (Fig. 4). The two structures together form the crista supraventricularis which separates the tricuspid and pulmonary valves. The septal part of the conus septum merges with the anterior ventricular septum between the two limbs of the trabecula septomarginalis (Fig. 4). The anterior part of the ventricular septum interposes between the infundibulum and the left ventricle, and subtends a considerable angle to the posterior interventricular septum, which is oriented between the ventricular inflow tracts (Fig. 4).

B: Fallot's tetralogy

These specimens are typified by counterclockwise rotation of the conus viewing it as from above. The aortic valve is dextroposed in relation to the atrioventricular orifices, and is anteriorly displaced so that it is no longer wedged between the atrioventricular valves (Fig. 5). Though the aortic valve is dextroposed, conal absorption has occurred in the mid-portion of the bulboatrioventricular ledge so that the mitral valve is in fibrous continuity with the aortic valve.

The valve overrides the anterior portions of the ventricular septum, and a large defect is present between the partially reoriented primary foramen and the right ventricle. In addition to conal rotation, anterior deviation of the conus septum is present. This is indicated by the septal insertion of the conus septum being anterior to the anterior limb of the trabecula septomarginalis which therefore forms the floor of the defect, covering the crest of the anterior septum (Fig. 5). Since the conus septum is rotated and anteriorly deviated, it no longer contributes to the ventricular septum, but forms a prominent supraventricular muscle mass. Its parietal insertion is also anteriorly deviated so that it is completely divorced from the right margin of the bulboatrioventricular ledge, which persists as a supraventricular muscle band separating the aortic and tricuspid valves. The degree of separation is dependent upon the degree of conal absorption. When absorbed, aortic-tricuspid continuity is present. When unabsorbed, a complete muscular ledge separates the two valves, and provides a muscular rim to the ventricular septal defect. Intermediate stages are present between these two extremes. The anterior deviation of the conus septum produces a very narrow infundibulum. However, its posterior wall is still separated from the left ventricle by a frontally oriented anterior septum (Fig. 5).

C: Double outlet right ventricle

The characteristic feature of these hearts is further counterclockwise rotation of the conus from the Fallot position, and absence of absorption in that part of the bulboventricular ledge between the aortic and mitral valves (Fig. 6). The actual degree of rotation of the conus varies within the subgroup of double outlet right ventricle, and they themselves constitute a spectrum. However, they can be divided into two main categories according to the position of the defect. The category nearer to the

FIG. 6 *Specimens of double outlet right ventricle. Fig. 6A and B show right and left ventricular views of a specimen with a subaortic defect. Note that the septal insertion (SI) of the conus septum (CS) is left posterior, and fuses with the anterior septum above the trabecula septomarginalis, separating the pulmonary outflow tract (POT) from the defect* (arrow). *The parietal insertion (PI) is right anterior. Note also that the right margin of the bulboatrioventricular ledge forms a second muscular crest separating the tricuspid and aortic valves. Fig. 6B illustrates the pulmonary artery separated from the left ventricle by the frontally oriented anterior septum (CS). The defect is between anterior and posterior (PS) septa. The arrow indicates the bulboatrioventricular ledge separating the mitral and aortic valves in the roof of the defect. Fig. 6C and D show similar views of a specimen with subpulmonary defect. Note that in this specimen the septal insertion (SI) of the conus septum (CS) is to the mid-portion of the bulboatrioventricular ledge, so that the septum separates the defect* (arrow) *from the aorta. The floor of the defect is the same, namely the trabecula septomarginalis reinforcing the anterior septum, but its roof has changed. This is well illustrated by Fig. 6D, where the conus septum is visible in the roof of the defect. The bulboatrioventricular ledge is seen separating the mitral valve from the pulmonary valve in this specimen* (arrow).

Fallot conal position has the great arteries in either side-by-side position or the aorta slightly posterior. This conal position is reflected by the orientation of the conus septum, which runs more or less in the sagittal plane of the heart. Its septal insertion is posterior and is to the anterior septum, merging between the limbs of the trabecula septomarginalis (Fig. 6).

From this situation the septum runs as a supraventricular structure anteriorly and rightwards to the free wall of the infundibulum. The defect therefore opens beneath the aorta, which is separated from the tricuspid valve by the right margin of the bulboatrioventricular ledge, which forms a second supraventricular structure. The ledge may be complete or may be absorbed to allow aortic-tricuspid continuity to occur. The proximity of the aortic valve to the defect is governed by the degree of absorption of the ledge. The trabecula septomarginalis and anterior septum are normally arranged, and the pulmonary artery arises from relatively normal infundibulum, which is anteriorly related to the left ventricle (Fig. 6).

When the defect is subpulmonary, the arteries are either side by side, or the pulmonary artery is slightly posterior. This further counterclockwise rotation of the conus is reflected by the position of the conus septum. The septal insertion is no longer to the anterior septum but is to the bulboatrioventricular ledge in a position above the posterior septum. From this situation the septum runs anteriorly and leftwards to the anterior wall of the infundibulum. The aorta is, therefore, separated from the defect by the conus septum, and is separated from the tricuspid valve by the right part of the bulboatrioventricular ledge. The septal insertion may also be attached to the posterior septum, or in some intermediate forms may be to the bulboatrioventricular ledge above the mid-point of the defect. In the latter case the defect opens into the right ventricle beneath both great arteries. Because of this type of septal insertion, the primary defect opens to the left beneath the pulmonary valve, and is bounded by the anterior septum inferiorly (reinforced by the trabecula septomarginalis), the left part of the bulboatrioventricular ledge superiorly, and the conus septum and central fibrous body posteriorly (Fig. 6). The anterior part of the interventricular septum is usually still oriented in a frontal plane, but if the left part of the bulboatrioventricular ledge is partially absorbed then the pulmonary valve may override the anterior septum. The differentiating feature between the two major groups of double oulet right ventricle is the roof of the defect. In the subaortic type the conus septum is to the left posteriorly; in the subpulmonary type the septum is to the right (R. Van Praagh, 1974, personal communication).

D: Transpositions

a) With concordant atrioventricular relations

This group also shows a wide variety of anatomical features, and some of the specimens resemble very closely the type of double outlet right ventricle with subpulmonary defect. Indeed, some cases cannot be clearly assigned to either category and are subsequently described as intermediate specimens. The transpositions most closely resembling double outlet right ventricle with subpulmonary defect all have a ventricular septal defect in identical position to the double outlet right ventricle specimens. The difference between them is that in the transpositions absorption of the left margin of the bulboatrioventricular ledge has occurred to allow mitral-pulmonary fibrous continuity. Furthermore, the anterior portion of the septum is observed to be oriented in the sagittal plane, so that the pulmonary artery is to its left. The conus septum is oriented as in double outlet right ventricle with subpulmonary defect, but the parietal portion is usually better developed and overlaps the anterior septum (Fig. 7A–C). Thus, when the defect is viewed from the right it opens beneath the prominent conus septum, but appears to be opening beneath the tricuspid valve (Fig. 7B). When viewed from the left it is clearly seen that the defect is between the conus septum and the anterior ventricular septum, and this is confirmed by sectioning the heart.

Although this arrangement is usually found with the pulmonary artery posterior, it can also be observed with the great arteries side by side, and with both sides of the bulboatrioventricular ledge separating the semilunar and atrioventricular valves. The arrangement of the conus septum and anterior septum is as described above (Fig. 7D–F).

When transposition is associated with an intact ventricular septum the pulmonary artery is usually in a posterior position (Fig. 8A), though it is occasionally observed side by side with the aorta. In these specimens the conus septum is less easily seen, and on the right side merges into the right part of the bulboatrioventricular ledge in a manner similar to the normal crista supraventricularis (Fig. 8E). When viewed from the left, the left side of the bulboatrioventricular ledge is usually completely absorbed and pulmonary-mitral fibrous continuity is present. The pulmonary valve overrides the anterior part of the ventricular septum which is oriented in a similar plane to the posterior septum (Fig. 8F). In these specimens it is occasionally possible to find a small membranous septum,

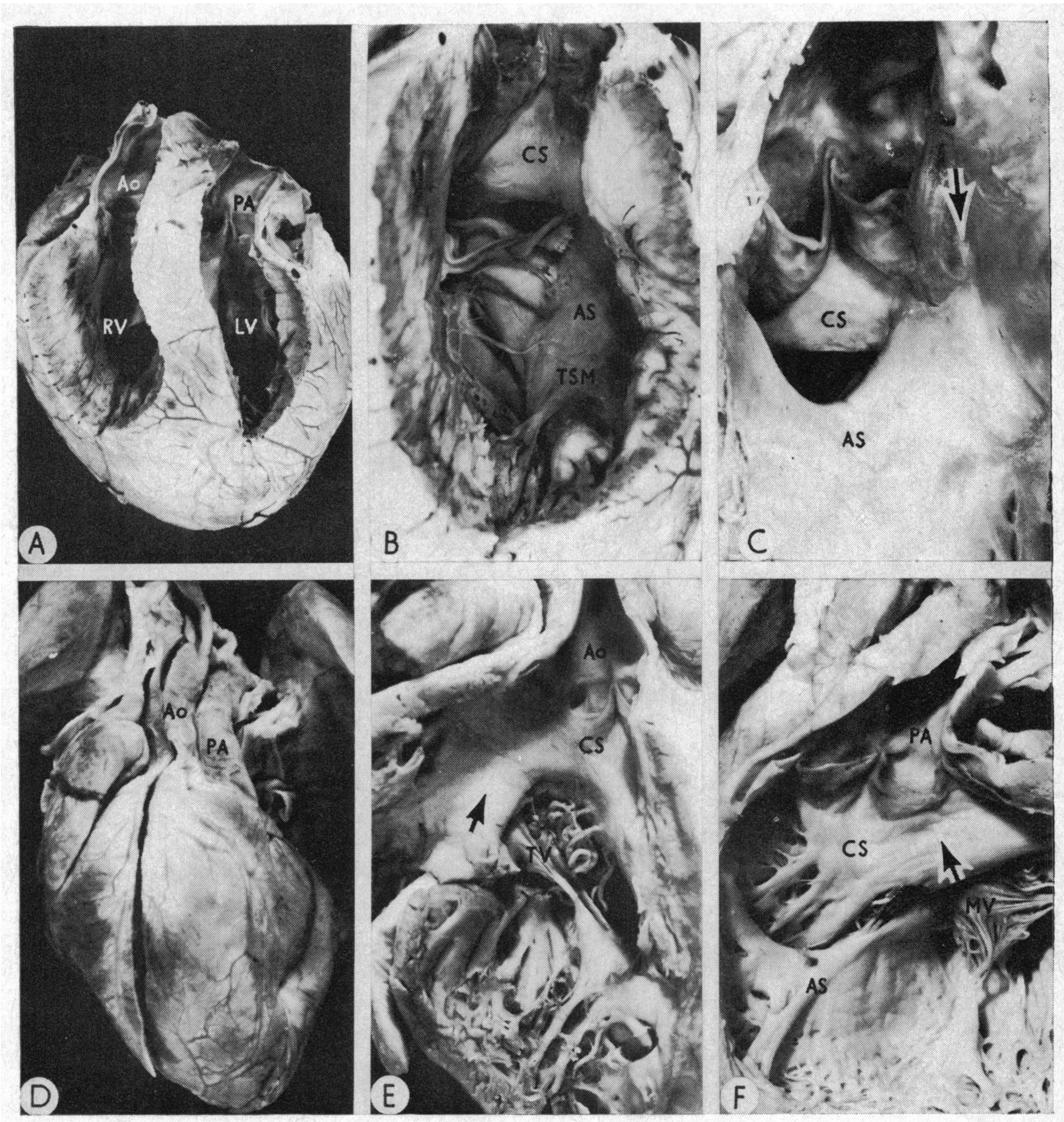


FIG. 7 *Photographs of transposition specimens with anterior defects. Fig. 7A–C show a specimen with mitral-pulmonary fibrous continuity. In 7A the sagittal orientation of the conus septum is demonstrated, and removal of the subpulmonary wall provided direct access to the left ventricle (compare with Fig. 6B). Fig. 7B shows the right ventricular view of the defect which is situated above the anterior septum and the trabecula septomarginalis, but below the conus septum. The left ventricular view (7C) confirms the relation of the defect to these septa, and demonstrates that the pulmonary valve overrides the anterior septum, though it is in fibrous continuity with the mitral valve* (arrowed). *Abbreviations as for previous figures. Fig. 7D–F demonstrate a similar specimen with bilateral conus. The views are directly comparable, and the defect is similarly related to conal and anterior ventricular septa. The septal insertion of the conus septum is clearly to the mid-point of the bulboatrioventricular ledge, and the persisting portions of ledge* (arrows) *separate the semilunar and atrioventricular valves, producing bilateral supraventricular muscle crests.*

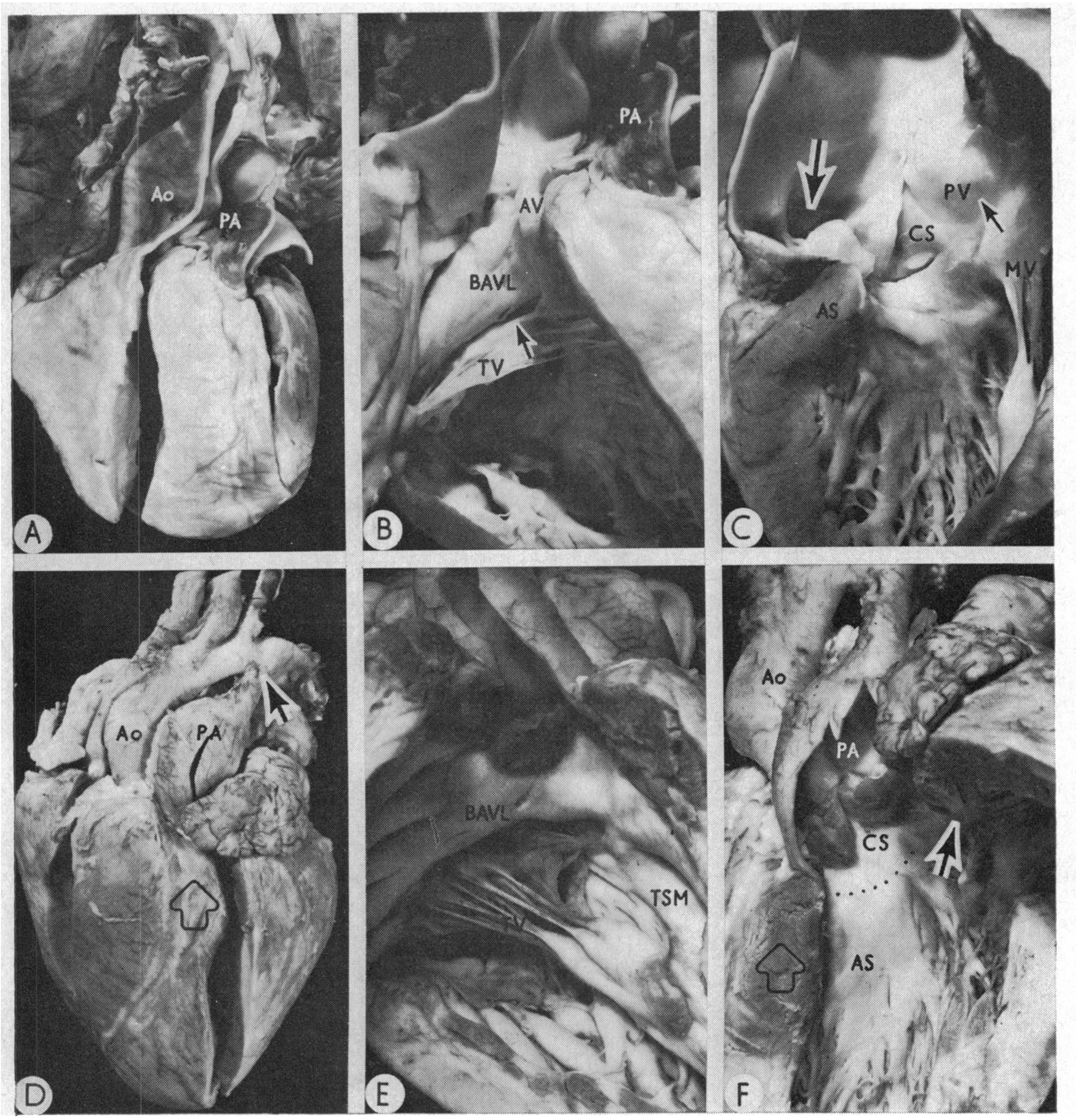


FIG. 8 *Photographs of specimens with transpositions demonstrating the closure of the defect by apposition of the conus and anterior septa. Fig. 8A–C show a specimen with a slit-like defect which demarcates the impending fusion between the conal and ventricular septa (Fig. 8C). The opening on the right side is beneath the bulboatrioventricular ledge* (arrow, *Fig. 8B*). *In Fig. 8C it is also demonstrated that the pulmonary artery overrides the anterior septum* (large arrow) *but that mitral-pulmonary continuity is present* (small arrow). *Fig. 8D–E demonstrate a specimen with intact septum. The open arrows (8D, 8F) indicate the relation between the subpulmonary ventricular wall and the left ventricle. The anterior septum is oriented sagittally in this specimen (compare Fig. 8C, 8F). The dotted line in Fig. 8F indicates the fusion point of conal and ventricular septa, and the arrow indicates tenuous mitral-pulmonary fibrous continuity. Though the structure in Fig. 8E separating aortic and tricuspid valves resembles the normal 'crista', it is in fact composed solely of the bulboatrioventricular ledge. Abbreviations as for previous figures.*

but usually the conus septum fuses directly with the central fibrous body.

More rarely it is possible to find specimens with a defect in the position of this membranous septum. This defect is situated between the conus septum, which is itself fused to the anterior septum, and the central fibrous body and posterior septum. In all these specimens the anterior wall of the left ventricle is the anterior cardiac wall itself, and a left-sided infundibulum is not seen. However, the trabecula septomarginalis is usually a very prominent feature of the right side of the anterior septum and overlies the right side of the conus septum (Figs. 7, 8).

b) With discordant atrioventricular relations All these specimens possess the feature that the bulboventricular loop does not correspond to the atrial situs. Thus, the morphological right atrium communicates with the morphological left ventricle, and is separated from it by a morphological mitral valve (Fig. 9A). The conus in these specimens is also inverted, but its morphology, apart from the inversion, is similar to that observed in transposition with concordant atrioventricular relations. The aorta is anterior to the pulmonary artery, but because of the inversion the aorta is left-sided and the pulmonary artery is right-sided. The conus septum is oriented from right anterior to left posterior, with the septal insertion again being posterior (Fig. 9B). The anterior septum is again deviated towards the conus septum and merges with its left side, but in most specimens evidence remains of the cleft between the two (Fig. 9B). Occasionally this cleft persists as a complete defect between the aortic infundibulum and the pulmonary outflow tract. The more usual defect in these specimens, however, represents a malorientation between the posterior interventricular and the atrial septa, and is positioned beneath the septal cusps of the atrioventricular valves and is posterior to the conus. Because of the inversion, it is the left margin of the bulboatrioventricular ledge which persists and separates aortic and tricuspid valves, while extensive absorption of the right margin permits pulmonary-mitral continuity (Fig. 9B).

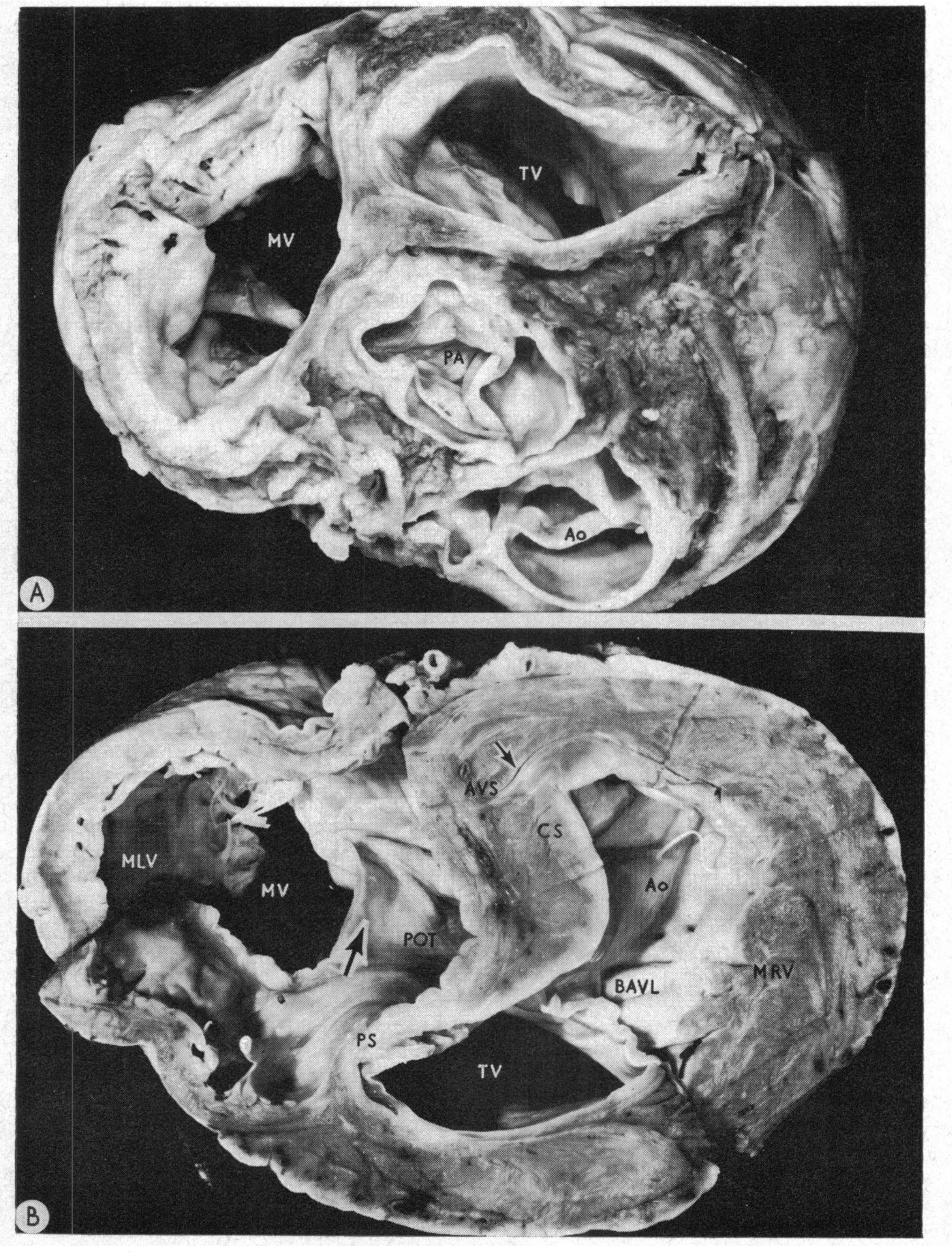
c) 'Posterior' transposition These specimens constitute an interesting subgroup of transpositions with concordant atrioventricular relations. The distinguishing feature is that the aortic valve is posterior to the pulmonary valve, and is in fibrous continuity with the mitral valve through a small 'membranous' type of defect. The lateral margin of the valve is separated from the tricuspid valve by the right side of the bulboatrioventricular ledge; the greater part of the aortic orifice is above the right ventricle. The conus septum is oriented as in the more usual transpositions, and is merged with the deviated anterior septum as described above. The pulmonary artery arises to the left of the conus septum, and is completely above the left ventricle. It is separated from the mitral valve by the persisting left portion of the bulboatrioventricular ledge which forms a substantial supraventricular muscle bar.

These specimens will be described in detail in a further communication devoted entirely to their morphology, embryogenesis and significance (Wilkinson *et al.*, 1974).

E: Intermediate specimens

It has been indicated that the main difference between double outlet right ventricular specimens with subpulmonary defect and complete transpositions with defects between the conus septum and anterior septum is the relation of the pulmonary artery to the anterior septum. When the artery is predominately above the right ventricle but overrides the septum, it is described as double outlet right ventricle; when predominately above the left ventricle and overriding the septum it is described as transposition. However, we have examined some specimens in which the pulmonary artery is situated above the anterior septum and we are therefore describing these as intermediate. Most of these cases override the septum since it is deviated rightwards while the conus septum is still arranged as in the double outlet right ventricle with subpulmonary defect specimens. However, an additional factor is increased absorption of the left side of the bulboatrioventricular ledge, since the separation between pulmonary and mitral valves is reduced to a thin muscular ridge (Fig. 10D, E).

One specimen was of particular interest in that, though the great arteries were arranged as in complete transposition with intact septum, the conus was arranged as in double outlet right ventricle with subpulmonary defect, and the pulmonary artery overrode a normally situated anterior septum, arising equally from right and left ventricles (Fig. 10C–D). A well-formed left margin of the bulboatrioventricular ledge was present which separated mitral and pulmonary valves (Fig. 10C). Though the anterior septum was normally oriented, it was poorly formed, and its crest was low down in the ventricular mass (Fig. 10C). A final specimen was also of great interest. This case had all the features of double outlet right ventricle with uncommitted defect, and both semilunar valves were separated from the atrioventricular valves by the persisting bulboatrioventricular ledge. However, the conus septum was a relatively poorly formed structure, and both the great arteries were found to override the anterior septum so that both could be considered to possess a biventricular origin (Fig. 11A–C). This specimen was, therefore, interpreted as an intermediate between double outlet right ventricle and double outlet left ventricle.



Discussion

As a result of our investigation of bulboventricular malformations, we have concluded that the specimens studied constitute a spectrum of anomalous development. Though most cases can be classified within presently defined conditions, some specimens were observed with features of two conditions occupying adjacent positions on the postulated spectrum. These specimens in themselves are strong evidence for the existence of a spectrum between Fallot's tetralogy and complete transposition. This exact spectrum was previously defined by Lev and his associates (1972) in terms of pure anatomical observations. While our anatomical findings are in complete agreement with theirs, they further demonstrate that the unifying feature of the spectrum is the gradual transition in position of the embryological structures described in the first part of this study (see Fig. 2). A diagrammatic representation of those changes is given in Fig. 12. Such an approach, based upon embryological observations, is in no way original to the investigation of bulboventricular malformations. In a similar fashion, Van Mierop and Wiglesworth (1963a) were able to establish a spectrum of anomalies from the normal heart to double outlet right ventricle. They considered that the spectrum represented faulty transfer of the posterior artery to the primitive ventricle, coupled with persistence of the conoventricular flange. However, they did not consider that transposition represented an extension of this process as the anatomical observations of Lev *et al.* (1972) suggest, but correlated that anomaly with abnormal formation of the conotruncal ridges (Van Mierop and Wiglesworth, 1963b). In contrast, Goor and Edwards (1973) have also described the spectrum from double outlet right ventricle to complete transposition in terms of transfer of the anterior artery to the primitive ventricle, and have interpreted this part of the spectrum also to represent conal maldevelopment. Our findings are in accord with the latter concept, and we consider the entire spectrum to reflect variations in position of conal structures, coupled with some change in position of the anterior ventricular septum. We therefore endorse the 'conal development hypothesis' of Van Praagh (1973a, b) and in view of the controversy still surrounding this topic (Van Mierop, 1971; Angelini and Leachman, 1973) it is important to set out in some detail our conclusions drawn from the presently described results. We will subsequently consider what we believe to be the significance of our findings to the nomenclature of congenital heart disease.

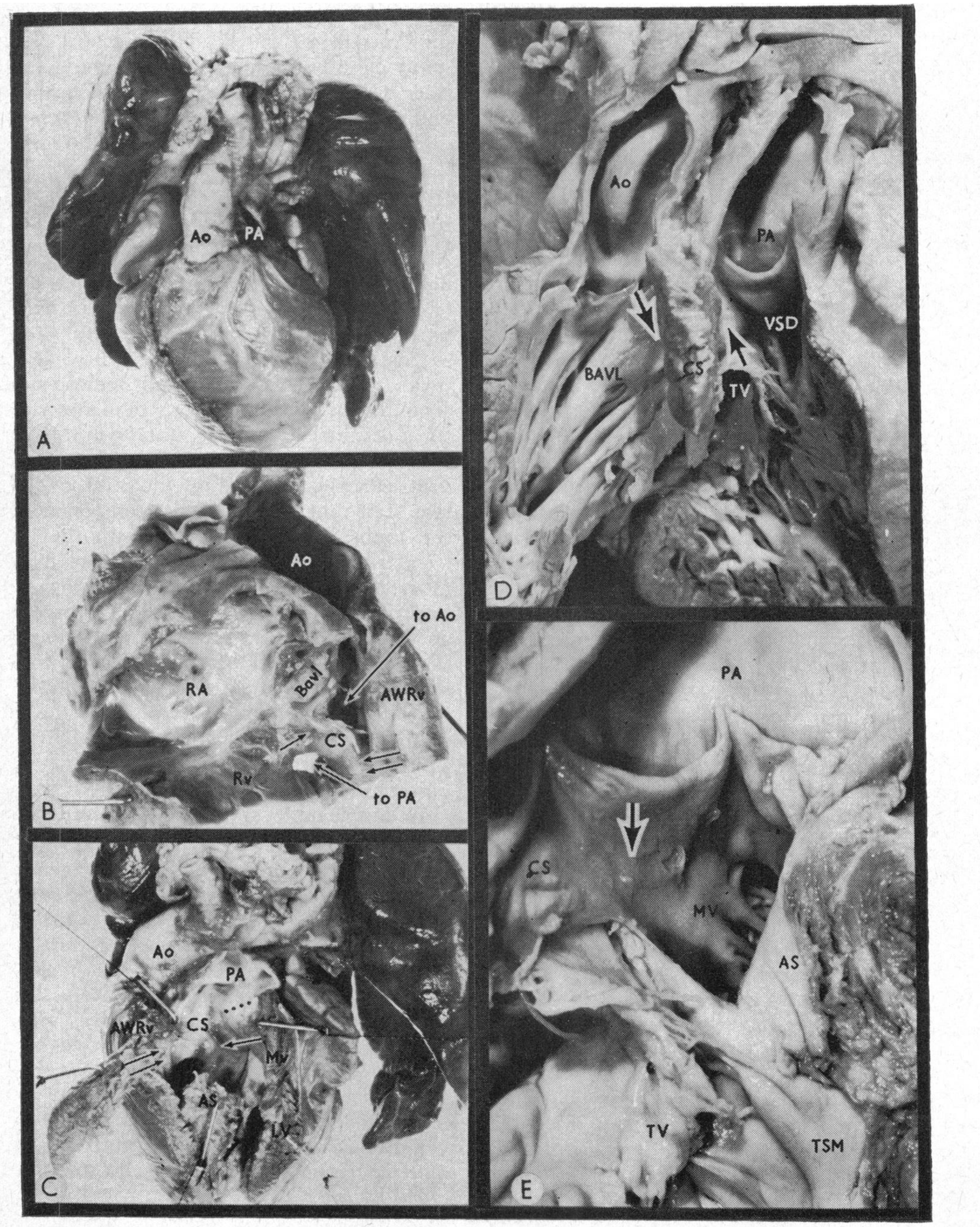
Evidence supporting the 'conal development hypothesis'

All the specimens that we have studied show evidence of rotation of conal structures. In the first part of our study (Anderson *et al.*, 1974) we avoided the use of 'conus' since it is a controversial term among embryologists. However, it has more general usage among pathologists and clinicians, and the term 'conus' is presently used to describe structures developed from our 'distal bulbus'. Similarly, the structure we will describe as the bulboatrioventricular ledge is the infolded wall of the primitive heart tube, and its bulbar component is part of the conus. It is synonymous with the 'conoventricular flange' described by other investigators (Van Mierop and Wiglesworth, 1963a, b). We believe that the conal rotation observed in the anomalous hearts is reflected by variations in position of the conal septum. This structure possesses septal and parietal insertions, and in the normal heart these insertions correspond to the positions of the conal ridges. Thus, the septal insertion is sinistroanterior and the parietal insertion is dextroposterior (Fig. 12).

In double outlet specimens, however, the parietal

FIG. 9 *Photographs of a specimen of classically corrected transposition. Fig. 9A shows the heart viewed from above after the removal of the atrial chambers and the great arteries. The mitral valve (MV) is right sided and the tricuspid valve (TV) left sided. Note that the pulmonary artery (PA) is posterior and to the right. It lies within the anteroposterior extent of the mitral valve. The aorta (Ao) is anterior and left sided and is separated from the tricuspid valve by the left margin of the bulboatrioventricular ledge. Fig. 9B is the interior view of the same heart after removal of the inferior part of the ventricular chambers. Note that the morphologically right ventricular wall (MRV) (left sided) is thicker than that of the right-sided morphologically left ventricle (MLV). The ventricular septum (AVS, PS) is inclined to the left, with its concavity towards its morphologically left ventricle. Note that the anterior segment (AVS) is separated from the conus septum (CS) by a cleft* (small arrow). *The pulmonary valve (POT) is in fibrous continuity with the mitral valve* (large arrow) *while the tricuspid valve is separated from the aortic valve by the left portion of the bulboatrioventricular ledge.*

insertion is anterior to, and in approximately the same sagittal plane as, the septal insertion. Therefore rotation in counterclockwise direction (viewed from above) of over a right angle has occurred. It is significant that the orientation of the conus septum in these specimens is identical to the postulated orientation of the conus ridges following 'lack of conal inversion' (Goor *et al.*, 1972, Fig. 4). We therefore endorse the opinion of Goor and Edwards (1973) that double outlet right ventricle represents 'lack of embryonic conal inversion'. Since the original normal conal inversion is dependent upon the looping of the bulboventricular segments of the heart tube, it is likely that 'lack of conal inversion'



reflects an abnormality during the looping process.

However, normal conal inversion does not produce a situation in which the aorta, or posterior conus, is above the primitive ventricle. Instead, it produces a situation in which the aortic conus is posterior to the pulmonary conus (though slightly to its right). Normal shift of the aorta to the left (primitive) ventricle is then dependent upon the absorption of the bulboatrioventricular ledge. There is a difference of opinion as to whether conal absorption is a primary event or secondary to leftward shift of the conoventricular junction (Goor *et al.*, 1972). In our opinion (Anderson *et al.*, 1974) conal absorption was a primary process, since we were unable to judge if leftward migration of the conus was entirely produced by conal shift, or whether it reflected lateralization of the right atrioventricular orifice.

Be that as it may, following conal absorption, which is agreed to be an embryological fact (Butler, 1952; Asami, 1969; Goor *et al.*, 1972; Anderson *et al.*, 1974), the primary bulboventricular foramen is reoriented to form the aortic outflow tract, and mitral-aortic fibrous continuity is established. The process of conal absorption is therefore an essential prerequisite in producing the anomaly of Fallot's tetralogy, which can be considered to represent lesser degrees of 'lack of conal inversion' than double outlet right ventricle. The lack of conal inversion would produce the dextroposed aorta, but conal absorption is necessary to produce an overriding aorta and mitral-aortic fibrous continuity. The lack of inversion also explains why absorption is possible in this condition between the aortic and tricuspid valves. Should such absorption not occur, then the two valves are separated by the persistent right margin of the bulboatrioventricular ledge. This can be stated with confidence since it is also known that the conus septum is deviated anteriorly in Fallot's tetralogy to produce the infundibular stenosis (Van Mierop and Wiglesworth, 1963a; Goor, Lillehei, and Edwards, 1971; Becker, Connor, and Anderson, 1974). Degrees of variation in the features of lack of conal inversion, conal absorption, and anterior deviation of the conus septum would explain the intermediate specimens observed between Fallot's tetralogy and double outlet right ventricle. Though we have not examined any specimens, it is likely that greater degrees of conal inversion and conal absorption coupled with lesser degrees of anterior deviation would produce the intermediate specimens described by Van Mierop and Wiglesworth (1963a) between Fallot's tetralogy and ventricular septal defect with overriding aorta (Eisenmenger complex). It is also likely that the same factors would produce a spectrum between the Eisenmenger complex and the normal heart which would include so-called 'infracristal' septal defects.

As indicated by Van Mierop and Wiglesworth (1963a) therefore, our observations support the concept of a spectrum representing faulty transfer of the posterior conus. We also agree with Van Mierop and Wiglesworth (1963a) that the structure separating aortic and atrioventricular valves in double outlet right ventricular specimens is the unabsorbed bulboatrioventricular ledge (or conoventricular flange).

However, our findings also indicate that the conus septum is oriented in identical fashion in transposition specimens as it is in double outlet right ventricular specimens. This is particularly well seen in specimens with large anterior defects, where the septal insertion is directly posterior to the parietal insertion (Fig. 12). Our findings further indicate that intermediate specimens exist between the categories of double outlet right ventricle with subpulmonary defect and complete transposition as

FIG. 10 *Illustrations of specimens intermediate between double outlet right ventricle with subpulmonary defect and 'complete' transposition in which the pulmonary artery is directly above the anterior septum (AS).*

In the specimen illustrated in Fig. 10A–C the arteries are oriented as in 'complete' transposition (Fig. 10A), but the anterior septum is frontally oriented (Fig. 10C) and a bilateral conus is present. The dots indicate this conus, which is the left margin of the bulboatrioventricular ledge, in Fig. 10C. The subpulmonary ventricular wall in this instance is part of the right ventricle (AWRV). The conus septum is oriented as in double outlet right ventricle specimens (compare Fig. 6). The single arrow is the septal insertion and the double arrows indicate the parietal insertion. Fig. 10D–E illustrate a similar specimen in which the arteries are oriented as in double outlet right ventricle specimens (Fig. 10D). However, the anterior septum is almost in the sagittal plane and is beneath the pulmonary valve (Fig. 10E). The conus septum is again oriented as in double outlet right ventricle specimens, and its septal insertion to the bulboatrioventricular ledge is illustrated in Fig. 10D (between arrows). *The arrow in Fig. 10E indicates the attenuating ledge between mitral and pulmonary valves. Abbreviations as for previous figures.*

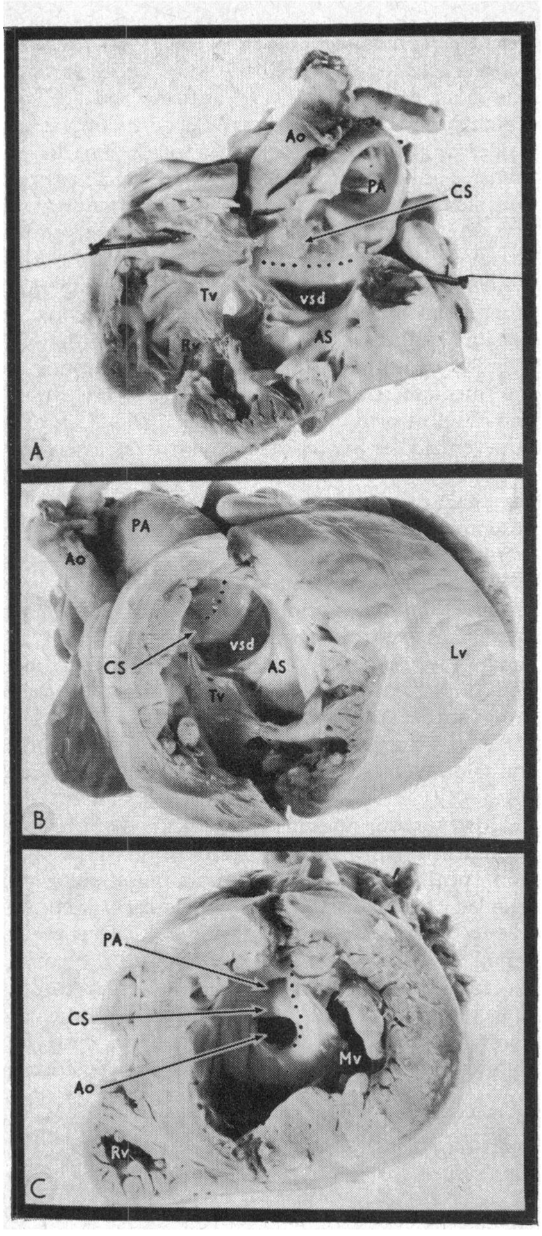


FIG. 11 *Intermediate specimen between double outlet right ventricle and double outlet left ventricle. The vessels are oriented as in double outlet right ventricle specimens, but the conus septum is a thin structure attached to the mid portion of the bulboatrioventricular ledge (Fig. 11A). The defect therefore opens beneath both arteries (Fig. 11B), and both arteries straddle the left ventricle and the anterior septum (Fig. 11C). However, the persistence of the ledge* (dotted line) *prevents semilunar – atrioventricular valvular continuity. Abbreviations as for previous figures.*

indicated by Lev *et al.* (1972) and Goor and Edwards (1973). Indeed in some cases we found it impossible to assign a specimen to either category. The observations, therefore, demonstrate that the specimens represent a spectrum characterized by transfer of the anterior artery to the primitive ventricle. We believe that during this transfer the primary foramen becomes reoriented to form the pulmonary outflow tract from the primitive ventricle in a manner directly comparable with that described during transfer of the posterior artery. The vital part of the spectrum, therefore, is that which converts the primary foramen from a subaortic to a subpulmonary position. This mechanism is clearly indicated by our observations of double outlet right ventricular specimens.

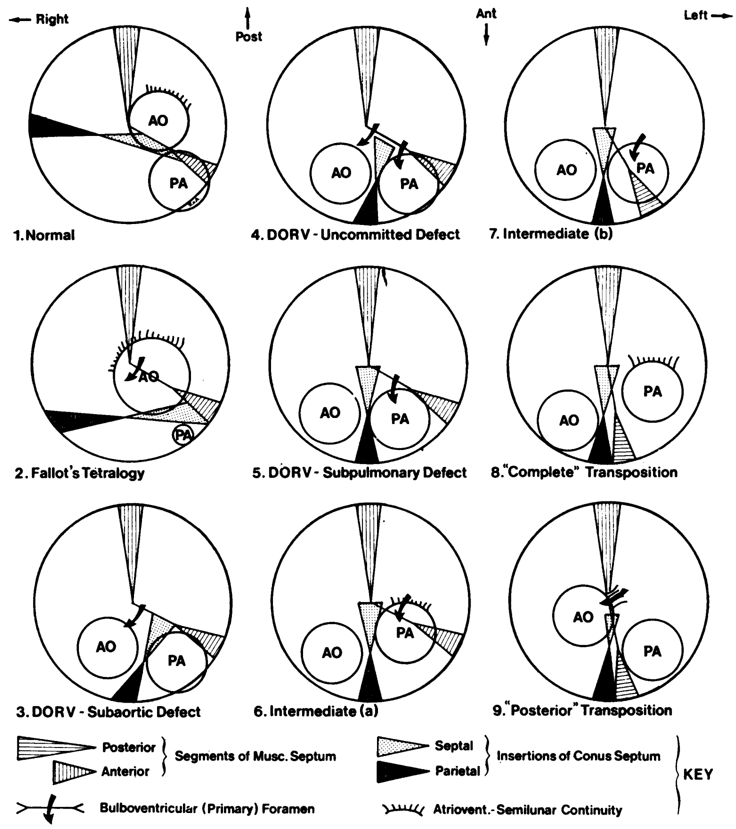
In the type of double outlet right ventricle with subaortic defect, representing the non-reoriented primary foramen, the defect is bounded superiorly by the intermediate segment of the bulboatrioventricular ledge and to the left by the conus septum (see Fig. 6, 12). The floor of the defect is the anterior septum reinforced by the trabecula septomarginalis. In the type of double outlet right ventricle with subpulmonary defect, the floor of the defect is the same. In contrast, the conal septum is now inserted to the right of the defect and the roof is formed by the left margin of the bulboatrioventricular ledge (see Fig. 6, 12). Thus the vital change involves the septal insertion of the conus septum, and transfers the primary defect from a subaortic to a subpulmonary position. The exact mechanism of this process cannot be elucidated by our study. However, it is possible that it represents further 'lack of conal inversion' or even conal inversion to the left. This is suggested by the finding that in double outlet right ventricle with subaortic defect the aorta is generally slightly posterior while with subpulmonary defects the pulmonary artery tends to be slightly posterior. This is also reflected in the orientation of the conus septum itself, but the shift of the septal insertion would automatically produce this change in orientation. Since change in position of the arteries can be produced by subsequent conal absorption, this evidence is tentative.

Be that as it may, our findings demonstrate that once the defect is established in the subpulmonary position, the pulmonary artery can be transferred to the left ventricle. However, unlike the situation in transfer of the posterior artery, which was accomplished solely by conal absorption (or leftward migration of the conoventricular flange), our findings suggest that an additional mechanism is involved. This mechanism is anterior and rightward deviation of the anterior segment of the ventricular septum. Goor and Edwards (1973) again explain this part of the spectrum on the basis of leftward shift of the conoventricular flange. We were unable to find any evidence of this shift when we used the atrioventricular orifices as our reference point. When the anterior septum is considered as a reference point there is no doubt that in double outlet right ventricular specimens it is to the left of the pulmonary artery, whereas in transposition specimens it is to the right of the artery. Our observations indicate, however, that rather than representing leftward conal migration, this represents rightward migration of the septum itself. This is demonstrated by the fact that the aorta is similarly related to the tricuspid valve in both double outlet right ventricle and transposition specimens. The conus septum is similarly related to both these structures in both categories. The anterior septum, in contrast, is almost at right angles to the posterior septum in double outlet right ventricle specimens, and its anterior extent is some distance from the conus septum; in transposition specimens it is in line with the posterior septum and its anterior extent abuts against the conus septum. Thus, in double outlet right ventricle specimens a subpulmonary infundibulum is present, and a pin inserted through the anterior cardiac wall beneath the pulmonary artery would traverse the infundibulum and anterior septum before entering the left ventricle. In transposition specimens the pin would pass directly into the left ventricle. This concept of anterior and rightward shift of the anterior septum also explains why intermediate specimens can exist in the presence of a bilateral conus, and why complete transposition with side-by-side arteries can exist with a bilateral conus. In both these situations, rather than the left margin of the bulboatrioventricular ledge migrating posteriorly during conal absorption, the anterior septum can be considered to have migrated anteriorly beneath a static conus. We are unable to explain why the septum should be so deviated, but our observations lead us to the conclusion that it, rather than the bulboatrioventricular ledge, undergoes migration. The ledge is of course absorbed during the process of transfer of the pulmonary artery but our findings indicate that this absorption produces migration in a posterior rather than a leftward direction. We are similarly unable to decide upon the relative importance of conal rotation, conal absorption, and septal migration, respectively.

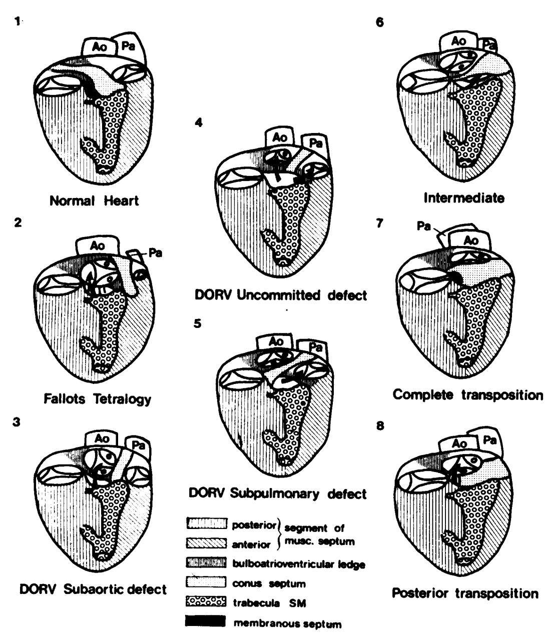
It is likely that the contributions of each process vary in different specimens, producing the wide variation in position of the arteries, the state of the bulboatrioventricular ledge and the overriding observed in transposition specimens. As a result of our study, we have concluded that the ventricular septal defect in transposition specimens is related in a similar fashion to the subpulmonary defect in double outlet right ventricle as is the isolated, so-called 'infracristal' defect to the subaortic defect in double outlet right ventricle specimens. The magnitude of the defect in transposition is dependent upon the degree of fusion between the conus septum and the anterior ventricular septum. When unfused a large anterior defect exists. When partially fused the defect is placed between the anterior and posterior ventricular septa and is directly comparable to the usual 'infracristal' defect. This space in transposition with intact septum is blocked by either fibrous tissue forming a membranous septum or by direct apposition of the muscular conal and ventricular septa. We believe that similar combinations of conal rotation, conal absorption, and septal migration explain the anomalies of double outlet left ventricle and posterior transposition, while similar processes associated with atrioventricular discordance produce the anomaly of 'corrected' transposition. 'Posterior' transposition is considered in greater detail elsewhere (Wilkinson *et al.*, 1974).

Conal development hypothesis versus straight septum hypothesis

The hypothesis relating conal maldevelopment to transposition is by no means recent, since Keith (1909) suggested that abnormal atrophy of the pulmonary conus and abnormal growth of the aortic conus would produce the anomaly. However, this concept took as its starting point the normal orientation of the conal ridges during normal development. As Harris and Farber (1939) indicated, this process produces an anterior pulmonary artery rather than a left-sided pulmonary artery, and absorption from this position would not be possible. This viewpoint was confirmed by the first part of our study (Anderson *et al.*, 1974) which showed that the formation of the sinistroanterior ridge automatically excluded the pulmonary artery from the left ventricle. Another objection to the hypothesis was that conal absorption was not considered to be a proven embryological fact. Thus, Paul, Van Praagh, and Van Praagh (1968) indicated that they had considered and discarded a conal absorption hypothesis for this very reason, indicating at the same time that Butler (1952) had suggested that absorption was an absolute event in the chick heart. Instead they proposed their conal growth hypothesis, since they considered that transposition specimens established growth of the aortic conus as an anatomical fact. None the less, this concept was not acceptable embryologically, since it assumed that the pulmonary artery originated above the primitive


Right
Post
Ant
Left
AO
PA
1. Normal
4. DORV - Uncommitted Defect
7. Intermediate (b)
2. Fallot's Tetralogy
5. DORV - Subpulmonary Defect
8. "Complete" Transposition
3. DORV - Subaortic Defect
6. Intermediate (a)
9. "Posterior" Transposition
Posterior
Anterior
Segments of Musc. Septum
Septal
Parietal
Insertions of Conus Septum
KEY
Bulboventricular (Primary) Foramen
Atriovent.-Semilunar Continuity

A


1
Ao
Pa
Normal Heart
2
Fallots Tetralogy
3
DORV Subaortic defect
4
DORV Uncommitted defect
5
DORV Subpulmonary defect
6
Intermediate
7
Complete transposition
8
Posterior transposition
posterior
anterior
segment of musc. septum
bulboatrioventricular ledge
conus septum
trabecula SM
membranous septum

B

ventricle, a situation occurring during normal development only at the straight tube stage, when conotruncal septation is absent. Since then, Goor *et al.* (1972) have demonstrated the importance of normal conal inversion, while Asami (1969), Goor *et al.* (1972), and ourselves (Anderson *et al.*, 1974) have shown the existence of conal absorption in the human embryo.

It is significant that this theory of conal absorption was carefully worked out in the earlier part of this century, culminating in the work of Pernkopf and Wirtinger (1933). Indeed, Lev and Saphir (1937) postulated a theory of embryogenesis for complete transposition based upon conal absorption and inversion which is in close accord with the more recent study of Goor and Edwards (1973) and this investigation. Despite these careful studies, as has been pointed out by Paul *et al.* (1968), a conal origin for the maldevelopment of complete transposition was not accepted. However, we consider that in view of the recent studies it is now possible to state that conal absorption can occur from side-by-side conal positions following lack of normal conal inversion, and that the concept is not based upon the arrest of 'normal' embryology.

Recent evidence has suggested that the embryological basis of the straight septum hypothesis is less sound. This concept, originally proposed by Quain (1844) and subsequently adhered to by Von Rokitansky (1875), De la Cruz and Da Rocha (1956), and Van Mierop and Wiglesworth (1963b), states that transposition is produced by straight rather than spiral fusion of the conotruncal ridges. However, the reconstructions of Los (1968) have shown that, though formed in spiral fashion, the conotruncal ridges fuse in straight fashion. This finding has been subsequently endorsed by Goor *et al.* (1972) and ourselves (Anderson *et al.*, 1974). Anatomical evidence also contends against the straight septum hypothesis.

It would be expected that straight formation of the septum would connect the anterior aorta to the normal anterior and left-sided conus. It is well established that the aortic conus is rarely to the left in 'complete' transposition with situs solitus. Similarly the straight septum does not provide for the development of all eight forms of transposition listed by Harris and Farber (1939). Van Mierop and Wiglesworth (1963b) answered this point by stating that all these forms did not exist since they were embryological impossibilities, yet all have received recent adequate documentation, and all are explainable in terms of the conal development hypothesis. In our opinion, therefore, it is now the straight septum hypothesis rather than the conal development hypothesis which is based upon questionable premises. Van Mierop and Gessner (1972) summed up the controversy by stating that transposition could not be considered to represent arrested normal development. However, they were prepared to accept double outlet right ventricle as persistence of the embryological stage at which both arteries are above the primitive bulbus. We have already stated that the conal development hypothesis no longer assumes arrested development, but states abnormal development. Of more importance is the fact that double outlet right ventricle cannot be considered to represent arrested development, since the double outlet right ventricle specimens in no way resemble a normal stage of development of the heart. Instead they represent the same abnormal development that produces transposition. In our view, therefore, and in view of the evidence now available, it is reasonable to propose that the mechanism producing double outlet right ventricle is also responsible for producing complete and other forms of transposition. It must be stated that Angelini and Leachman (1973) have studied examples of 'intermediate' specimens and concluded that they bear no relation to transposition, but constitute a separate entity which they term partial distortion. This opinion is in contrast not only to the present study but also to the careful investigations of Lev *et al.* (1972) and Goor and Edwards (1973). Furthermore, the concept has been criticized at length by Van Praagh (1973b) and we endorse his views.

Significance to nomenclature of congenital heart disease

The described observations illustrate the difficulties encountered in providing a strict definition of any

FIG. 12 *Diagram of the spectrum illustrated by the pathological specimens. Fig. 12A is constructed using transverse sections, Fig. 12B represents the septal surface of the right ventricle. Note that the spectrum involves counterclockwise rotation of the conus septum, and clockwise rotation of the anterior septum. It is completed by conal absorption and apposition of the conal and ventricular septa. For the purposes of this diagram we have considered the posterior septum as being in the sagittal plane, and illustrated rotation of the other septa with reference to this plane. This is not intended to indicate that these structures occupy these positions in the living subject, but merely to demonstrate their varying interrelations.*

particular malformation. Rather than 'defining' the malformation it seems to be more appropriate to list its common features, while appreciating that specimens or cases may not possess all these features, and indeed may possess features of another malformation. It follows that we do not consider it suitable to become involved in arguments which question the 'trueness' of double outlet right ventricle in the presence of overriding of the pulmonary artery. Indeed, the question of overriding is one of the major 'bones of contention' in this field. The recent suggestion of Kirklin *et al.* (1973) provides a suitable answer to this particular problem. They define a double outlet situation as that in which more than one and a half arteries arise from the same ventricle, and this is equally applicable to right and left ventricles. However, some form of classification is essential for correlative studies and we have constructed the guidelines enumerated in the Table.

Thus, we consider that mitral-aortic fibrous continuity or discontinuity is a good criterion for differentiating Fallot's tetralogy from double outlet right ventricle on pathological grounds, while accepting that it would be more difficult to implement from an angiographic standpoint and that cases can exist with mitral-aortic continuity in which more than half the aorta is above the right ventricle. The definition we use of transposition, in contrast, is equally valuable in a clinical context since it is essentially a functional classification. The concept of defining arteries as transposed when placed across the septum is the original definition as given by Farre (1814). More recently this concept was adopted by Elliott *et al.* (1963), but it has been brought into prominence by Van Praagh *et al.* (1971) with no little controversy (Van Mierop, 1971; Van Praagh, 1971). Van Praagh has expanded the concept to account for malposition of the arteries.

In his opinion, transposition is only present when both great arteries are placed across the septum to arise from inappropriate ventricles. When only one artery is placed across the septum, or either artery is incorrectly related to its appropriate ventricle, then malposition of the arteries is said to exist.

The advantages of this system are, 1) it is based upon functional criteria, 2) it is easily applicable to angiographic usage, 3) it is easy to interpret and understand, and 4) it removes such non-specific and paradoxical terms as 'partial transposition' and 'anatomically corrected transposition', as indicated by Wilkinson and Acerete (1973).

Another non-specific term which is responsible for the production of much confusion is the 'crista supraventricularis'. In the first part of our study, we showed that this structure, which we considered to represent the tissue between the pulmonary and tricuspid valves in the normal heart, was developed from two sources. These were first the right margin of the bulboatrioventricular ledge and secondly the parietal insertion of the conus septum. We also agreed with Van Praagh (1968) that the 'septal band' or trabecula septomarginalis should not be considered as part of the crista. Both these points were illustrated in the study of Pernkopf and Wirtinger (1933). It is particularly significant that they considered that the trabecula septomarginalis was not derived from the bulbar ridges, but this contention was not supported by Lev and Saphir (1937). It has been substantiated by the embryological studies of both Goor *et al.* (1972) and ourselves.

The present observations substantiate the embryological results and illustrate the reasons for the confusion surrounding the term 'crista supraventricularis'. All three components mentioned above, namely bulboatrioventricular ledge, conus septum, and trabecula septomarginalis have been shown to occupy widely differing positions in the hearts studied. The trabecula septomarginalis, however, has never been observed in a supraventricular position, this finding substantiating the opinion that it should not be considered as part of the 'crista'. Both the right margin of the bulboatrioventricular ledge and the conus septum have been shown to form supraventricular muscle masses. In some cases they are evident simultaneously as in double outlet right ventricle and some Fallot specimens. In further hearts, for example 'posterior' transpositions and double outlet right ventricle with subpulmonary defect, both right and left margins of the bulboatrioventricular ledge together with the conus septum can exist as supraventricular masses. In these situations, or in complete transposition with bilateral conus, the left margin of the bulboatrioventricular ledge forms a supraventricular crest above the left ventricle, and Van Praagh *et al.* (1971) have named this the left ventricular 'crista'. Thus all these masses can be, and have been, referred to as the 'crista', as has the 'septal band'. It is little wonder that confusion arises relative to this term.

In our opinion, confusion would be removed if the term 'crista supraventricularis' were restricted to usage in the normal heart. The supraventricular masses in congenitally malformed hearts could then be described in terms of their embryological origin, depending upon one's opinion of the latter. Thus, the conus septum would be described as such, though the 'parietal band' is an alternative at present in widespread usage. Confusion also surrounds this term, however, since Lev *et al.* (1972) distinguish the two components of the normal crista as 'parietal band 1' and 'parietal band 2' when they exist separately as in double outlet right ventricle. We would rather describe the muscle tissue separating semilunar and atrioventricular valves as the bulboatrioventricular ledge or conoventricular flange, since we consider it is this structure that forms the 'parietal band 2' of Lev *et al.* (1972). Other authors, however, consider these muscle bars to represent the proximal end of the conus septum, but if this is so it would be preferable if they were described as 'proximal conus septum' rather than 'proximal crista' (Rosenquist *et al.*, 1973) or 'parietal band 2' (Lev *et al.*, 1972). It follows that if this approach were adopted, then ventricular septal defects would no longer be definable in terms of the 'crista'. In our opinion this would be an advantage rather than a disadvantage, since one is never sure which 'crista' is being taken as a particular reference point.

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References

Anderson, R. H., Wilkinson, J. L., Arnold, R., and Lubkiewicz, K. (1974). Morphogenesis of bulboventricular malformations. I: Considerations of embryogenesis in the normal heart. *British Heart Journal*, **36**, 242.

Angeleni, P., and Leachman, R. D. (1973). Pulmonary artery originating anteriorly from the left ventricle. *American Journal of Cardiology*, **32**, 840.

Asami, I. (1969). Beitrag zur Entwicklung des Kammerseptums im menschlichen Herzen mit besonderer Berücksichtigung der sogenannten Bulbusdrehung. *Zeitschrift für Anatomie und Entwicklungsgeschichte*, **128**, 1.

Becker, A. E., Connor, M., and Anderson, R. H. (1974). Tetralogy of Fallot – a morphometric and geometric study. *American Journal of Cardinology*. In the press.

Butler, J. K. (1952). An experimental analysis of cardiac loop formation in the chick. M.A. Thesis, University of Texas.

De la Cruz, M. V., and Da Rocha, J. P. (1956). An ontogenetic theory for the explanation of congenital malformations involving the truncus and conus. *American Heart Journal*, **51**, 782.

Elliott, L. P., Neufeld, H. N., Anderson, R. C., Adams, P., and Edwards, J. E. (1963). Complete transposition of the great vessels. I. An anatomic study of sixty cases. *Circulation*, **27**, 1105.

Farre, J. R. (1814). *Pathological Researches. Essay 1. On Malformations of the Human Heart*, p. 28. Longman, Hurst, Rees, Orme and Brown, London.

Goor, D. A., Dische, R., and Lillehei, C. W. (1972). The conotruncus. I. Its normal inversion and conus absorption. *Circulation*, **46**, 375.

Goor, D. A., and Edwards, J. E. (1973). The spectrum of transposition of the great arteries: with specific reference to developmental anatomy of the conus. *Circulation*, **48**, 406.

Goor, D. A., Lillehei, C. W., and Edwards, J. E. (1971). Ventricular septal defects and pulmonic stenosis with and without dextroposition. Anatomic features and embryologic implications *Chest*, **60**, 117.

Harris, J. S., and Farber, S. (1939). Transposition of the great cardiac vessels (with special reference to the phylogenetic theory of Spitzer). *Archives of Pathology*, **28**, 427.

Keith, A. (1909). The Hunterian lectures on malformations of the heart. *Lancet*, **2**, 359, 433, and 519.

Kirklin, J. W., Pacifico, A. D., Bargeron, L. M., and Soto, D. (1973). Cardiac repair in anatomically corrected malposition of the great arteries. *Circulation*, **48**, 153.

Lev, M., Bharati, S., Meng, C. C. L., Liberthson, R. R., Paul, M. H., and Idriss, F. (1972). A concept of double outlet right ventricle. *Journal of Thoracic and Cardiovascular Surgery*, **64**, 271.

Lev, M., and Saphir, O. (1937). Transposition of the large vessels. *Journal of Technical Methods*, **17**, 126.

Los, J. A. (1968). Embryology. In *Textbook of Paediatric Cardiology*, p. 1. Ed. by H. Watson. Lloyd-Luke, London.

Paul, M. H., Van Praagh, S., and Van Praagh, R. (1968). Transposition of the great arteries. In *Textbook of Paediatric Cardiology*, p. 582. Ed. by H. Watson. Lloyd-Luke, London.

Pernkopf, E., and Wirtinger, W. (1933). Die transposition der Herzostien – ein Versuch der Erklärung dieser Erscheinung: Die Phoronomie der Herzentwicklung als morphogenetische Grundlage der Erklärung. *Zeitschrift für Anatomie und Enwicklungseschichte*, **100**, 563.

Quain, R. (1844). *The Anatomy of the Arteries of the Human Body and its Applications to Pathology and Operative Surgery*. Taylor and Walton, London.

Rosenquist, G. C., Sweeney, L. J., Stemple, D. R., Christianson, S. D., and Rowe, R. D. (1973). Ventricular septal defect in tetralogy of Fallot. *American Journal of Cardiology*, **31**, 749.

Van Mierop, L. H. S. (1971). Transposition of the great arteries. I. Clarification or further confusion? *American Journal of Cardiology*, **28**, 735.

Van Mierop, L. H. S., and Gessner, I. H. (1972). Pathogenetic mechanisms in congenital cardiovascular malformations. *Progress in Cardiovascular Diseases*, **15**, 67.

Van Mierop, L. H. S., and Wiglesworth, F. W. (1963a). Pathogenesis of transposition complexes. II. Anomalies due to faulty transfer of the posterior great artery. *American Journal of Cardiology*, **12**, 226.

Van Mierop, L. H. S., and Wiglesworth, F. W. (1963b). Pathogenesis of transposition complexes. III. True transposition of the great vessels. *American Journal of Cardiology*, **12**, 233.

Van Praagh, R. (1968). What is the Taussig-Bing malformation? *Circulation*, **38**, 445.

Van Praagh, R. (1971). Transposition of the great arteries. II. Transposition clarified. *American Journal of Cardiology*, **28**, 739.

Van Praagh, R. (1973a). Conotruncus malformations. In *Heart Disease in Infancy – Diagnosis and Surgical Treatment*, p. 86. Ed. by B. G. Barratt-Boyes, J. M. Neutze, and E. A. Harris. Churchill Livingstone, Edinburgh.

Van Praagh, R. (1973b). Do side-by-side great arteries merit a special name? *American Journal of Cardiology*, **32**, 874.

Van Praagh, R., Perez-Trevino, C., Lopez-Cuellar, M., Baker, F. W., Zuberbuhler, J. R., Quero, M., Perez, V. M., Moreno, F., and Van Praagh, S. (1971). Transposition of the great arteries with posterior aorta, anterior pulmonary artery, sub-pulmonary conus and fibrous continuity between aortic and atrioventricular valves. *American Journal of Cardiology*, **28**, 621.

Van Praagh, R., and Van Praagh, S. (1966). Isolated ventricular inversion: a consideration of morphogenesis, definition and diagnosis of non-transposed and transposed great arteries. *American Journal of Cardiology*, 17, 395.

Von Rokitansky, K. F. (1875). *Die Defekte der Scheidewände des Herzens*. Braumüller, Vienna.

Wilkinson, J. L., and Acerete, F. (1973). Terminological pitfalls in congenital heart disease. *British Heart Journal*, 35, 1166.

Wilkinson, J. L., Arnold, R., Anderson, R. H., and Acerete, F. (1974). Pathological features of 'posterior' transpositions. In preparation.

Addendum

In the first part of this study (Anderson *et al.*, 1974) we gave a misinterpretation of the reason for Paul *et al.*, (1968) proposing a conal growth hypothesis rather than one based upon conal absorption. We suggested that this was due to the fact that Harris and Farber (1939) had declared the absorption hypothessis untenable. This was an erroneous statement on our part. As explained in the present article, Paul *et al.* (1968) proposed a growth hypothesis because it was supported by known anatomical facts, whereas at the time an absorption hypothesis was not adequately supported by embryological data.

Requests for reprints to Dr. R. H .Anderson, Department of Anatomy and Embryology, Institute of Child Health, Alder Hey Children's Hospital, Eaton Road, Liverpool, L12 2AP.